of this morpholino on production of Ret mRNA and PD morphogenesis will be discussed.

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Program/Abstract # 337

The role of Bicaudal-C in kidney development of *Xenopus* and mouse

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The RNA-binding molecule Bicaudal-C regulates embryonic development in *Drosophila* and *Xenopus*. Interestingly, mouse mutants lacking Bicaudal-C do not show early patterning defects, but instead develop severe polycystic kidney disease (PKD). This phenotype can be detected as early as E15.5 and is characterized by the formation of enlarged epithelial structures in the proximal tubules and the glomerulus of the metanephric kidney. It was not caused by increased proliferation, but rather impaired differentiation of the renal epithelial cells. To further investigate the molecular mechanism of Bicaudal-C in kidney development, we analyzed its function in the developing *Xenopus* pronephros. Inhibition of the translation of endogenous Bicaudal-C with antisense morpholino oligomers (*xBic-C-MO*) led to a PKD-like phenotype. Embryos lacking Bicaudal-C developed generalized edemas and dilated pronephric tubules and ducts. This phenotype was also caused by impaired differentiation of the pronephros. Molecular markers specifically expressed in the late distal tubule were absent in *xBic-C-MO*-injected embryos. Furthermore, Bicaudal-C was not required for primary cilia formation, an important organelle affected in PKD. However, *xBic-C-MO*-injected embryos exhibited changes in left-right patterning, another paradigm for cilia function. These data support the idea that Bicaudal-C functions downstream of a cilia-regulated signaling pathway. This pathway is important for proximal-distal patterning of the pronephros and regulates renal epithelial cell differentiation, which – when disrupted – results in PKD.

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***Pax2* and *Pax8* regulate branching morphogenesis and nephron differentiation in the developing kidney**

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The critical role of *Pax* genes during kidney development has been demonstrated by the analysis of *Pax2*$^{-/-}$ mouse embryos, which fail to form a metanephros. This early phenotype largely precluded the study of *Pax* genes during metanephric kidney development. In order to address the later role, we analyzed kidneys of *Pax2 Pax8* compound heterozygous embryos. Pax2 and Pax8 are closely related family members, which are coexpressed in the collecting duct and differentiating nephrons. *Pax2*$^{+/-}$ *Pax8*$^{+/-}$ kidneys are hypodysplastic and show a severe reduction in nephron and ureter tip number. The defect in nephron formation is accompanied by a strong decrease of *Lim1* expression, increased apoptosis and deficits in distal tubule differentiation. At the ureter tips, the expression of *Wnt11* is significantly downregulated. Taken together, these data reveal important roles for Pax2 and Pax8 in nephron differentiation and branching morphogenesis of the metanephros.

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Program/Abstract # 340

β-Catenin and MAPK/ERK signaling are both required for mesenchymal–epithelial transition (MET) in nephron formation

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The metanephros is formed from reciprocal interactions between the epithelial ureteric bud and the metanephric mesenchyme (MM), which is induced by the bud to convert to the epithelia of the nephron. Wnt signaling is essential in this process; however, the absence of activity from a b-catenin-activated transgene reporter (BAT-gal) in mouse MM or its derivatives suggests a noncanonical mechanism. Using an explant culture system, we found that glycogen synthase kinase-3b (GSK3b) inhibitors are potent inducers of MET. Furthermore, inhibitor treatment stabilized b-catenin, yielding distinct molecular forms which selectively bind to cadherins for cell adhesion or TCF for transcriptional activation, and activated a Topflash reporter. Disruption of b-catenin/cadherin complex formation with genetic constructs or neutralizing antibodies blocked MET, while a dominant-negative TCF had no effect. These studies suggest that cadherin/b-catenin complex formation, but not TCF activation, is required for epithelial conversion. In addition, inhibition of GSK3b blocked apoptosis, stimulated proliferation, and activated ERK phosphorylation in MMs. Furthermore, MAPK